Remarks

The Office Action mailed November 6, 2009, has been received and reviewed. Claims 1 and 8 having been amended, the pending claims are claims 1-17. Reconsideration and withdrawal of the rejections are respectfully requested.

With this response, amended claim 1 recites "[a] method for treating a patient having a nervous system injury associated with hemorrhage, the method comprising administering to the patient having a nervous system injury associated with hemorrhage an effective amount of a compound selected from the group consisting of a hydrophilic bile acid, a salt thereof, an analog thereof, and a combination thereof~~, wherein the nervous system injury is associated with hemorrhage~~" and amended claim 8 recites "[a] method for treating a patient having a nervous system injury associated with hemorrhage, the method comprising administering to the patient having an injury associated with hemorrhage an effective amount of a compound selected from the group consisting of ursodeoxycholic acid, a salt thereof, an analog thereof, and a combination thereof~~, wherein the nervous system injury is associated with hemorrhage~~."

As one can see from the marked up versions of the claims presented above, claims 1 and 8 have been amended so that the recitation "wherein the nervous system injury is associated with hemorrhage" at the end of the claim is repositioned to the preamble of the claim, at the location of the recitation "[a] method for treating a patient having a nervous system injury" to recite "[a] method for treating a patient having a nervous system injury associated with hemorrhage." Applicants submit that such an amendment raises no new issues for search or examination, as the recitation has already been fully searched and examined by the Examiner.

Further, the recitation "comprising administering to the patient" is amended, based on antecedent basis, to recite "comprising administering to the patient having a nervous system injury associated with hemorrhage." Again, Applicants submit that such an amendment raises no new

issues for search or examination, as the recitation has already been fully searched and examined by the Examiner.

Applicants respectfully request the entry and examination of amended claim 1 and 8.

The 35 U.S.C. §102 Rejection

The Examiner has maintained the rejection of claims 1-17 under 35 U.S.C. 102(b) as anticipated by Steer et al. (WO99/15179). Applicants continue to traverse this rejection.

According to MPEP § 2131 a "claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference."

Steer et al. (WO99/15179) does not expressly describe the claimed invention

Claims 1-17 are drawn to a methods "for treating a patient having a nervous system injury associated with hemorrhage, ***the method comprising administering to the patient having a nervous system injury associated with hemorrhage*** an effective amount of a compound selected from the group consisting of a hydrophilic bile acid, a salt thereof, an analog thereof, and a combination thereof" (claims 1-7) or "an effective amount of a compound selected from the group consisting of ursodeoxycholic acid, a salt thereof, an analog thereof, and a combination" (claims 8-17). As acknowledged by the Examiner, Steer et al. does not teach administering the claimed compounds for the treatment of patients having a nervous system injury associated with hemorrhage (see page 4, Final Office Action mailed November 6, 2009). Thus, Steer et al. does not expressly set forth each and every element of claims 1-17 and cannot anticipate claims 1–17. The reconsideration and withdrawal of this rejection under 35 U.S.C. 102(b) is requested.

Steer et al. (WO99/15179) does not inherently describe the claimed invention

In maintaining this anticipation rejection, the Examiner asserted "that the claimed methods are implicitly disclosed and inherently achieved by those taught by the reference" (see page 3,

Final Office Action mailed November 6, 2009); arguing that "[b]y disclosing methods of administering UDCA, GUDCA, or TUDCA to limit apoptosis associated with stroke, regardless of whether the stroke is of ischemic or hemorrhagic variety, the reference inherently discloses the treatment of nervous system injury associated with hemorrhage or hemorrhagic stroke, namely, neural cell death" (see bridging pages 4-5, Final Office Action mailed November 6, 2009) and that "[i]n other words, the methods disclosed in WO99/15179 anticipate the claimed methods because administering UDCA, GUDCA, or TUDCA to limit apoptosis associated with stroke comprises the same steps and inherently results in the treatment of a nervous system injury associated with hemorrhage or hemorrhagic stroke (i.e. neural cell death)" (see page 5, Final Office Action mailed November 6, 2009).

Applicants respectfully submit that the Examiner's position is incorrect and direct the Examiner to *Perricone v. Medicis Pharmaceutical Corp.* (77 USPQ2d 1321 (Fed Circ. 2005) (copy provided herewith) for the legal standard for the application of inherent anticipation to the new use of a known compound. In parallel with the facts and the holding in *Perricone v. Medicis Pharmaceutical Corp.*, Applicants submit that the issue is not whether hydrophilic bile acids **if administered** to a patient having a nervous system injury associated with hemorrhage would inherently treat that injury. Rather, the issue is whether Steer et al. discloses the administration of compounds "to a patient having a nervous system injury associated with hemorrhage" "for treating a patient having a nervous system injury associated with hemorrhage" (see the discussion in section [3] of *Perricone* (77 USPQ2d 1321, 1328 (Fed Circ. 2005)).

Claims 1-17 are drawn to "[a] method for treating a patient having a nervous system injury associated with hemorrhage, the method comprising administering to the patient having an injury associated with hemorrhage an effective amount of" the recited compounds.

As acknowledged by the Examiner, the teachings of Steer et al. are limited to "methods of limiting apoptosis (cell death) in a cell population by contacting such cells with the claimed compounds" (see page 3, Final Office Action mailed November 6, 2009) and methods

"for inhibiting apoptosis associated with nonliver disease in vivo, such as 'cardiovascular disease (e.g. stroke, myocardial infarction and the like'" (see page 4, Final Office Action mailed November 6, 2009)). Further, the discussion in Steer et al. of treating stroke injury is limited to the treatment of experimentally induced ischemic stroke (see page 16-17 of Steer et al.).

Applicants respectfully submit that the Examiner's assertion that Steer et al.'s disclosures of methods of limiting apoptosis and treating ischemic stroke injury inherently discloses the claimed methods of treating nervous system injury associated with hemorrhage is incorrect. As disclosed in the specification, "[a] nervous system injury is an injury of the nerves, which is characterized by the presence of hemorrhage. For example, the nervous system injury associated with hemorrhage could be a hemorrhagic stroke, a head trauma, a spinal cord injury, or a peripheral nerve injury" (see page 6, lines 1-4 of the specification). "Preferably, the injury is a hemorrhagic stroke, which is characterized by an actual bleed into the brain matter due to breakdown of blood vessel integrity. ***This is distinct from an ischemic stroke, which is characterized primarily by obstruction of blood flow into a prescribed area of the brain. Typically, ischemic strokes do not have associated hemorrhage***" (see page 6, lines 5-10 of the specification (emphasis added)). And, ***"[a]lthough the compounds described herein are known for the treatment of ischemic stroke it was unexpected that they could be used for the treatment of hemorrhagic stroke or other nervous system injuries because of the inherent injury associated with hemorrhagic stroke. It was not known whether cell death was associated with apoptosis, necrosis and/or necroptosis. Immediate cell death (which typically occurs in hemorrhagic stroke) is typically a result of necrosis, whereas delayed cell death (which typically occurs in ischemic stroke) is typically a result of apoptosis*** ((see page 6, lines 5-10 of the specification (emphasis added)).

Applicants submit that nothing in Steer et al. directs the skilled artisan to administer the recited compounds to a "patient having a nervous system injury associated with hemorrhage" "for treating a patient having a nervous system injury associated with hemorrhage." Likewise, Applicants submit that Steer et al. provides no showing that the claimed compounds would be

effective for "for treating a patient having a nervous system injury associated with hemorrhage." Thus, Steer et al. cannot inherently anticipate the methods of claims 1-17.

In essence, the Examiner argues that ischemic stroke and associated apoptosis allow one skilled in the art to conclude that nervous system injury associated with hemorrhage can be treated by the same methodology. Contrary to this erroneous view, ischemic stroke is a disease pathophysiologically different from hemorrhagic stroke, even though the term "stroke" is shared between the two. Ischemic brain injury is due to the occlusion of blood vessels in the brain, whereas hemorrhagic brain injury occurs when blood vessels burst. The bursting of blood vessels causes a release of blood directly to cells within the brain, and this direct contact of blood products with neural cells has a toxic effect leading to cell death. In contrast, the lack of blood flow to the brain associated with ischemic strokes initiates a different cascade of events. Blockage of blood flow causes oxygen deprivation leading to mitochondrial dysfunction. Mitochondria then release caspase c, which in turn initiates apoptosis. Other biochemical pathways are involved in ischemic brain injury. These include the release of excitotoxic neurotransmitters that cause excessive calcium influx into postsynaptic cells. Excess calcium then overwhelms mitochondria, leading to apoptosis. Given the above, one of ordinary skill would not equate a method for treating ischemic stroke in substance or scope with a method of treating hemorrhagic injury.

Again, Applicants submit that nothing in Steer et al. directs the skilled artisan to administer the recited compounds to a "patient having a nervous system injury associated with hemorrhage" "for treating a patient having a nervous system injury associated with hemorrhage." Likewise, Steer et al. provides no showing that the claimed compounds would be effective for "for treating a patient having a nervous system injury associated with hemorrhage." Thus, Steer et al. cannot inherently anticipate the methods of claims 1-17.

In view of the above discussion, the reconsideration and withdrawal of this rejection under 35 U.S.C. §102(b) is respectfully requested.

Summary

It is respectfully submitted that the pending claims 1-17 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives at the telephone number listed below if it is believed that prosecution of this application may be assisted thereby.

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The undersigned hereby certifies that this paper is being transmitted via the U.S. Patent and Trademark Office electronic filing system in accordance with 37 CFR §1.6(a)(4) to the Patent and Trademark Office addressed to the Commissioner for Patents, Mail Stop **AF**, P.O. Box 1450, Alexandria, VA 22313-1450,
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